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U1S S1053

(56) Documents Cited
GB 1483574 A EP 0139424 A2 EP 0138351 A2
US 4997100 A US 4421246 A US 4034884 A

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(54) **Adaptor, holder or container suitable for histology processing cassettes**

(57) An adaptor, holder or container for processing very small tissue samples in histology processing cassettes comprises a lid (1) and a base (2). The lid (1) and the base (2) may be engaged together to form a chamber therebetween. At least one and preferably both of the top and bottom walls of the chamber are perforate, for example by virtue of being made of fine mesh (8).

The lid (1) and the base (2) may be designed for either side of one to engage a respective side of the other, whereby in one engagement position a relatively deep chamber may be formed and in another a relatively shallow chamber.

The device is of suitable dimensions to fit in a tissue processing cassette.

FIG. 1

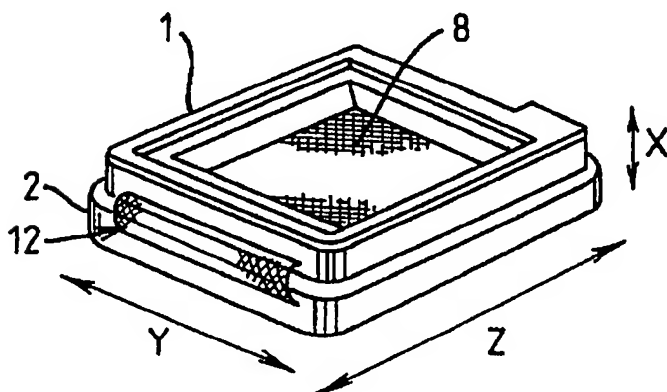
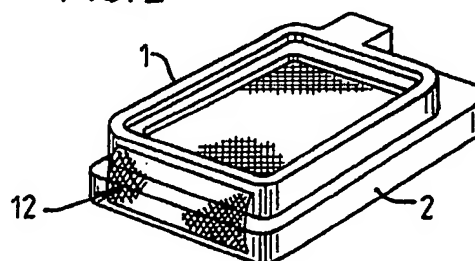


FIG. 2



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FIG. 1

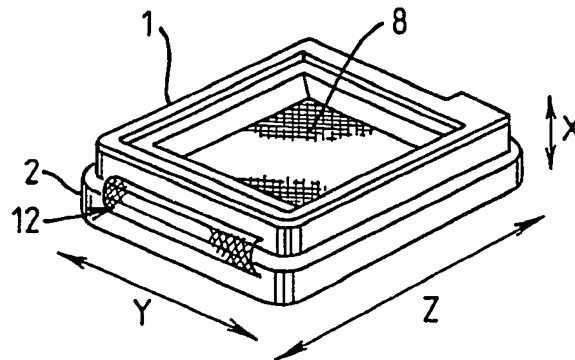


FIG. 2

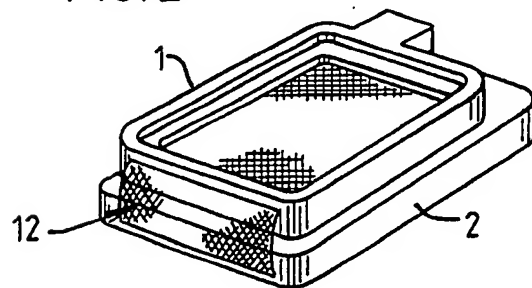


FIG. 3

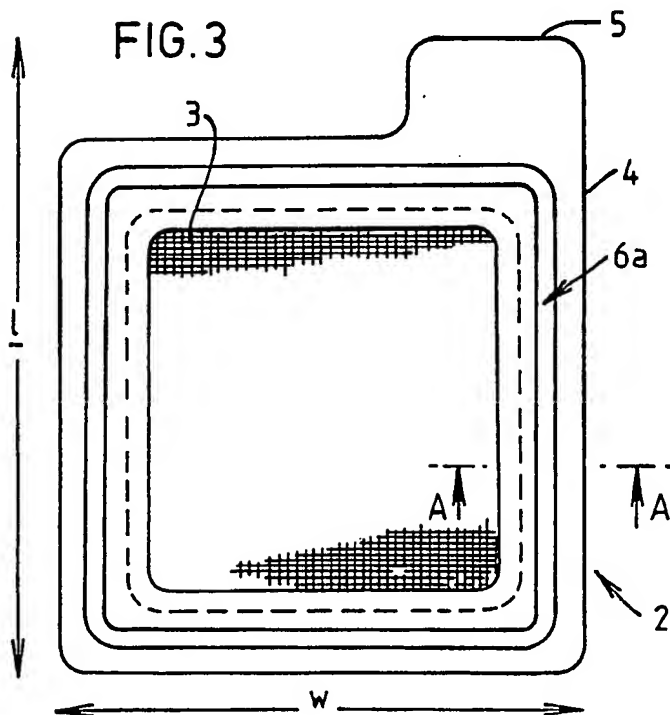


FIG. 4

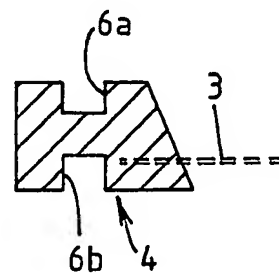


FIG. 5

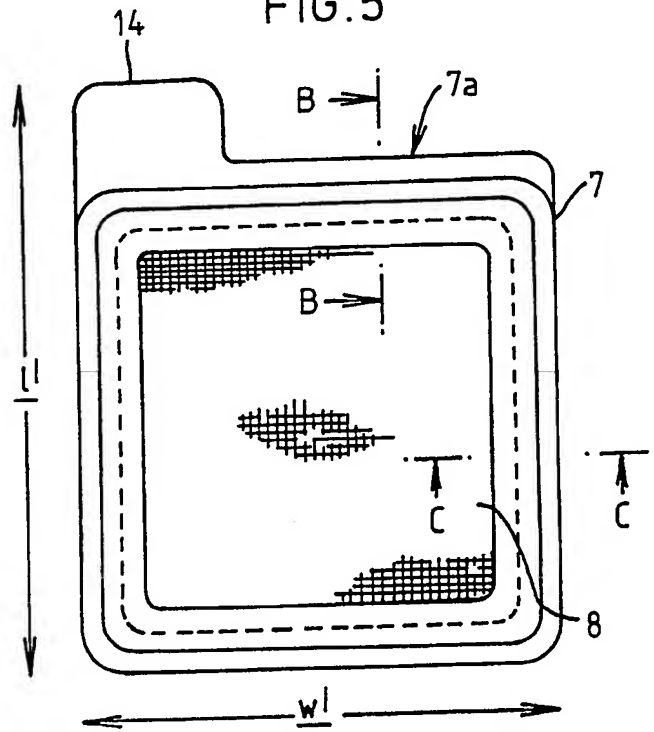


FIG. 6

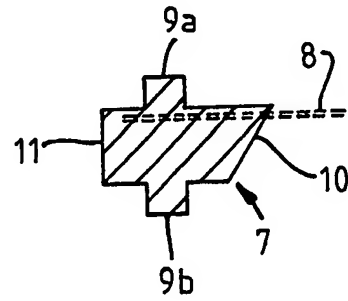


FIG. 7

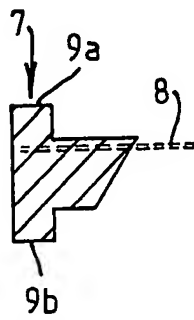
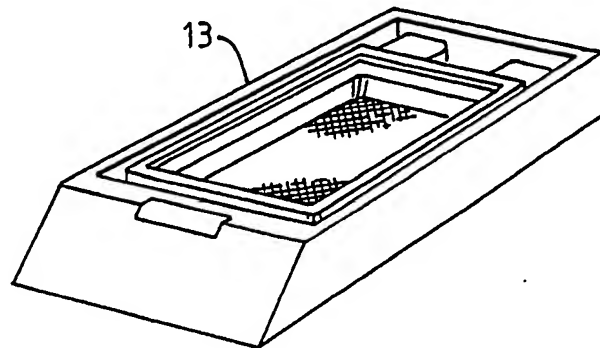


FIG. 8



CONTAINER

5 The present invention relates to a container for use in pathology to transport small tissue samples.

Biological tissues for histological examination are processed with several fluids to dehydrate the tissue and to clear the tissue of a suitable oil. The tissue is then
10 infiltrated with wax to provide it with the rigidity necessary for microtome slicing.

Tissues are conventionally processed using a processing cassette comprising an open-topped box with a perforated bottom wall and a perforated removable cover. The perforations of the box and cover are usually about 3 mm in diameter. Such
15 processing cassettes are described in GB 1230913 and US 3674396. Such processing cassettes are used with the cover in place as a tissue processing capsule and with the cover removed for embedding a specimen in paraffin.

Processing cassettes can be described as ubiquitous and are broadly of standard
20 size, since they are required to fit standard specimen holders of microtomes. Typically, processing cassettes have internal dimensions of 30-32 mm x 25-26 mm x 5 mm. Obviously, minor variations in size occur, dependent for example upon the wall thickness of the box. Processing cassettes with a plastics lid often have a continuous flange extending around the periphery of the lower face of the lid and
25 spaced from the peripheral edge of the lid so that the flange fits within the side wall of the box-like base. Such flanges are provided to rigidify the lid.

An increasing number of tissue samples are very small in size, for example having dimensions of less than 1 mm, and are therefore too small to be processed in a
30 standard processing cassette, since they would pass through the perforations of the lid and base. Various approaches have been adopted to enable small specimens to be processed in standard processing cassettes. For example, stainless steel mesh

may be inserted in the cassette or the tissue may be wrapped in porous wrapping paper such as tea bag tissue, toilet tissue or cigarette paper, for example. In some areas of the world there are used bags of woven polyamide (nylon). An alternative system has been developed using fine filter sponges but these have been found to cause artefacts and as a result are losing favour.

A problem which can arise in processing very thin tissue samples, for example skin, is that such specimens tend to curl up at the edges. Wrapping in porous paper does help to control such curling.

The apparatus and materials used hitherto for transporting and processing small tissue samples involve drawbacks, for example difficulty in handling, and it would be desirable to provide apparatus for transporting and processing small tissue samples for embedding in wax prior to slicing and microscopic examination.

It would also be desirable to provide apparatus for transporting and processing thin specimens which prevents or controls curling of the specimens.

In a first aspect, the invention provides an adaptor for insertion into a histology processing cassette to enable the cassette to be used for processing small tissue specimens. The adaptor is of suitable dimensions to be fitted in a processing cassette and it comprises a base and a lid to engage the base and define therewith a chamber to hold a tissue sample. The chamber has a bottom wall defined by a cross wall of the base and a top wall defined by a cross wall of the lid. At least one of the base and the lid comprises a peripheral frame defining therewithin an area across which is disposed a fine mesh secured to the frame and forming at least part of the cross wall of its associated lid or base.

Preferably, both the base and the lid comprise a peripheral frame defining therewithin an area across which is disposed a fine mesh secured to the frame.

In preferred embodiments the or each said peripheral frame is made by injection

moulding a thermoplastics material around a mesh such that a peripheral edge portion of the mesh is embedded in the moulded frame.

5 Preferably, the mesh has a pore size of no more than 1 mm and more preferably of no more than 500 μm . More typically, the pore size is from 40 to 400 μm . Preferably, the mesh is made of polyamide (nylon).

10 It is preferred that the base and the lid be interconnected by hinge means, for example mesh in one piece with the mesh of the at least one of the base and the lid comprising mesh.

15 Preferably, the adaptor further comprises locking means to hold the lid in the closed position. The lock means may comprise a male member on one of the base and the lid and a female member on the other of the base and the lid and adapted to engage lockingly with the male member, for example. The male member may comprise a continuous or discontinuous upstanding rib extending around a peripheral area of one of the base and the lid and the female member a continuous or discontinuous groove around a peripheral area of the other of the base and the lid and in which the rib is a press fit.

20 Preferably, the base and the lid are adapted to engage in two different relative positions, in one of which positions the height of the chamber is relatively large (e.g. 2-4 mm high) and in the other of which it is relatively low (e.g. 0.5-1.5 mm high). To this end, it is preferred to provide a holder wherein

25 (a) in one of the positions the lid engages the base with a first side of the lid facing thereto and in the other of the positions engages the base with a second side of the lid opposite the first facing the base, or

30 (b) in one of the positions the base engages the lid with a first side of the base facing thereto and in the other of the positions engages the lid with a second side of the base opposite the first facing the lid, or

- (c) at least when the lid and the base are hinged together, in one of the positions the lid and the base interengage with a first side of the lid facing a first side of the base and in the other of the positions they interengage with a second side of the lid facing a second side of the base.

The arrangement is such in any of these cases that in one of the positions the chamber is higher than in the other.

- 10 It is preferred that in adaptors embodying feature (a) the cross wall of the lid is disposed closer to one of said sides of the lid than to the other.

In adaptors embodying feature (b) the cross wall of the base is preferably disposed closer to one of said sides of the base than to the other.

- 15 In adaptors embodying feature (c) the cross wall of at least one of the base and the lid is preferably disposed closer to one of its sides than to the other.

- 20 Preferably, when the lid engages the base, an adaptor of the invention has overall dimensions of about 5 mm x 25 mm x 32 mm or less. The length and width of the lid may be reduced to enable the adaptor to be fitted in a processing cassette with a reinforced plastics lid without the lid of the adaptor interfering with the reinforcing flange of the cassette lid.

- 25 In another aspect the invention provides a tissue sample holder, comprising a base and a lid to engage the base and define therewith a chamber to hold a tissue sample, the base having a cross wall which forms the bottom wall of the chamber and the lid having a cross wall which forms the top wall of the chamber, at least one of said cross walls being a perforate, and the base and the lid being adapted to engage in two different relative positions, in one of which positions the height of the chamber is relatively large and in the other of which the height of the chamber is relatively small.
- 30

The relatively high chamber may be from 2 to 5 mm, e.g. 3 to 4 mm high, for example. The relatively low chamber may be 0.5 to 1.5 mm, e.g. 0.7 to 1 mm high, for example.

- 5 Preferably the or each perforate cross wall comprises a fine mesh. Preferably the holder is adapted to be fitted in a conventional processing cassette.

Other preferred features include the preferred features of the first aspect of the invention.

10

The invention provides in its third aspect a capsule for transporting small tissue samples and for processing them in a processing cassette, the capsule being adapted to fit in a processing cassette and comprising a base and a lid to engage the base, the cross wall of at least one of the lid and the base comprising a fine mesh.

15

Preferably, both the lid and the base have a cross wall comprising a fine mesh , e.g. with a pore size of up to 1 mm and more usually up to 500 μm , e.g. 40 to 400 μm . Preferably the lid and the base are connected together by hinge means; for example the capsule may comprise a single continuous web of mesh which forms the cross wall of both the lid and the base and interconnects the two as a hinge.

20

Preferably, the lid and the base can be interengaged in two different relative positions to form chambers of different height in the capsule. Preferably, at least one of the lid and the base is adapted for either of its opposed faces to engage the other of the lid and the base and its cross wall is closer to one of its faces than the other, such that the distance by which said cross wall is spaced from the cross wall of the other cross wall of the capsule depends upon which of said opposed faces engages the other part of the capsule.

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Preferably, the lid and the base are hinged together and the lid can be pivoted to

engage, suitably interlockingly, with either face of the base. Thus, in one closed position one pair of lid and base faces interengage whilst in the other closed position another pair of lid and base sides interengage. At least one and preferably both of the lid and base have cross walls closer to one of their faces than the other, such that the depth of the chamber formed within the capsule differs with the different pairs of interengaging faces.

Further included in the invention is a holder for tissue samples comprising a base and a lid to engage the base, the cross wall of at least one of the lid and the base being perforate and the lid and the base being capable of being interengaged in two different relative positions to form chambers of different height in the capsule. The holder may be used for transporting and/or processing tissue samples.

Preferably the or each perforate cross wall comprises a fine mesh.

Preferably the holder is adapted to fit in a processing cassette.

The present invention is further described by way of example only with reference to the accompanying drawings, in which:

Figure 1 is a perspective view of a tissue holder of the invention with the lid and base closed in a first position;

Figure 2 is a perspective view of the holder of claim 1 closed in a second position;

Figure 3 is a plan view of the base of the holder of Figure 1;

Figure 4 is a cross section along line A-A of Figure 3;

Figure 5 is a plan view of the lid of the holder Figure 1;

Figure 6 is a cross section along line B-B of Figure 5;

Figure 7 is a cross section along line C-C of Figure 5; and

Figure 8 is a perspective view of the holder of Figure 1 inserted in the body of a standard pathology processing cassette.

5

Figure 1 illustrates a capsule or holder to encapsulate small tissue samples such as, for example, small tissue biopsies and curettings taken from human or animal subjects and used for diagnostic purposes in cellular pathology. The holder comprises a lid 1 and a base 2. The lid 1 and the base 2 may be engaged together as shown in Figure 1 to form a chamber therebetween. At least one of the top and bottom walls of the chamber is perforate and normally comprises a web of fine mesh, for example the top wall 8 shown in Figure 1.

10

Figures 3 and 4 illustrate the base 2 of Figure 1 in more detail. The base 2 comprises a peripheral frame 4. The frame is suitably made of a plastics material. Within the frame there is defined an area across which is disposed the mesh 3. The mesh 3 suitably has a pore size of up to 1 mm and more often of from 40 μm to 400 μm e.g. 200 μm . The mesh 3, which is conveniently made of nylon, is secured to the frame 4 in a continuous region extending around the frame 4. In the illustrated embodiment, the frame 4 is injection moulded around the mesh 3 in one operation. In modified embodiments, the mesh 3 is adhered or welded to the frame 4, for example, rather than moulded in it. The mesh 3 is preferably not equidistant between the top and bottom surfaces of the frame 4 but displaced closer to one side of the frame than the other, as shown in Figure 4.

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The frame 4 is substantially uniform in cross section except in the region of a tab 5, which assists in handling of the holder, for example to open and close it. As shown in Figure 4, the frame 4 is generally H-shaped in cross-section, and has a continuous groove 6a formed in the top face and a continuous groove 6b formed in the bottom face. In other embodiments, the groove is discontinuous.

30

Figure 5, 6 and 7 illustrate the lid 1 of the holder. The lid 1 is similar to the base

2 in comprising a peripheral frame 7 which forms a border round a window spanned by a mesh 8 securely held to the frame 7. The lid 1 may be formed by injection moulding in the same manner as the base 2. The mesh 8 is preferably located closer to one of the top and bottom faces of the frame 7 than the other.

5

The frame 7 is substantially uniform in cross section along three of its sides but is optionally modified in cross section along one of its sides 7a which is provided with a tab 14. The tab 14 is for the same purpose as the tab 5 of the base 2.

10 Figure 6 illustrates the cross section of the frame 7 along the side 7a. The frame 7 is shown to have opposed upstanding ribs 9a, 9b on its top and bottom surfaces, intermediate the internal 10 and external 11 side edges of the frame 7. In Figure 7, the frame 7 on the other three sides of the lid is shown not to extend outwardly of the ribs 9a, 9b. However, the precise configuration of the frame 7 is a matter
15 of choice. The ribs 9a, 9b are complementary in cross section to the grooves 6a, 6b on the base 2.

The lid 1 and base 2 of the holder are preferably linked together, usually by a hinge means 12 (Figures 1 and 2). In preferred embodiments, the hinge means is
20 formed by mesh which is continuous with the mesh 3 and the mesh 8 of the base 2 and the lid 1, respectively; such a holder can be formed by injection moulding the base 2 and the lid 1 around the mesh in one operation. The lid 1 and the base 2 are preferably vertically aligned on the mesh, with the mesh displaced equally to one side of the centre line of both.

25

The holder illustrated in Figures 1 and 2 of the drawings is reversible, that is either surface of the lid 1 may engage the base 2. In Figure 1, the lid 1 and the case 2 are shown in a closed position with the mesh 8 of the lid 1 and the mesh 3 of the base 2 located relatively closely towards the other of the lid 1 and the
30 mesh 3. The lid mesh 8 and the base mesh 2 are therefore close together and define a chamber of small height, e.g. of about 0.7 to 1 mm in the illustrated embodiment. Such a narrow chamber is suitable for handling thin sections of

tissue which must be kept flat, for example skin biopsies.

5 In Figure 2, the lid 1 and base 2 are closed with the opposite faces engaged to those of the orientation of Figure 1. The lid mesh 8 and the base mesh 3 are separated by a greater distance than in the orientation of Figure 1, e.g. of 3 to 4 mm (say, 3.5 mm) in the illustrated embodiment and thicker samples can be held.

10 In the closed positions of Figures 1 and 2 the ribs 9a or 9b of the lid engage in a press fit in the grooves 6a or 6b of the base to lock the lid and the base together.

The drawings illustrate one embodiment of the invention and many modifications are possible. For example, in less preferred embodiments, only one of the lid and the base is provided with a mesh cross wall, the other cross wall being solid, for example.

15 Whilst it is preferred that the lid and the base be interengageable in two different positions providing chambers of different heights, as exemplified in the illustrated embodiment, this is not essential. In the case of "reversible" capsules, e.g. as shown in the drawings, it is particularly preferred that both the lid and the base be provided with mesh cross walls, to enable either to filter fragments of tissue from transport fluid.

20 In the case of non-reversible capsules, the external surface of the mesh (the surface on the exterior of the closed capsule) may be supported by a grid integral with the frame.

25 It is not critical that locking means be provided to hold the lid and the base in a closed position, although this is preferred. Convenient locking means comprise male and female members which are a press fit with one another. In some embodiments the locking means comprises a flexible clip. To provide effective locking, it is preferred to provide mating ribs and grooves, as illustrated, which may be continuous or discontinuous around the periphery of the lid and base.

The preferred holders of the invention are designed to be used in conventional processing cassettes as an adaptor to hold small tissue samples which are too small for such cassettes. To that end, when in the closed position, such preferred holders have maximum overall dimensions $X \times Y \times Z$ (see Figure 1) of approximately 5 mm x 25 mm x 32 mm. These dimensions allow some room for play within a processing cassette and may be increased slightly, e.g. by up to about 1 mm. A holder of the invention in the base 13 of a processing cassette is illustrated in Figure 8.

- 10 In the illustrated embodiment, the base 2 has a width w (Figure 3) of 25 mm and a length l of 30 mm. These dimensions normally allow for slight play, and could be increased by up to 1 mm for example. The lid may be of the same size but is preferably smaller to fit in a processing cassette with a reinforced plastics lid, and in the illustrated embodiment has a width w^1 of 23 mm and a length l^1 of 23 mm.
- 15 The height of the closed capsule is 5 mm.

The holder is made of material which is inert to processing fluids it is to contact. A suitable material is acetal.

- 20 A holder of the invention may be used as follows. A tissue sample, e.g. a needle biopsy, is placed in the base of the holder and the lid is closed. The holder is transported to a laboratory where it is placed in a processing cassette and processed for wax infiltration. The processed sample is removed from the holder and embedded in wax in the usual way. It will be appreciated that the holder may
- 25 also be used in other ways.

CLAIMS

1. An adaptor for insertion into a histology processing cassette to enable the cassette to be used for processing small tissue specimens, comprising a base and
5 a lid to engage the base and define therewith a chamber to hold a tissue sample, the chamber having a bottom wall defined by a cross wall of the base and a top wall defined by a cross wall of the lid, at least one of the base and the lid comprising a peripheral frame defining therewithin an area across which is disposed a fine mesh secured to the frame and forming at least part of the cross
10 wall of said at least one of the base and the lid, the adaptor being of suitable dimensions to be fitted in a processing cassette.
2. An adaptor of claim 1, wherein both the base and the lid comprise a peripheral frame defining therewithin an area across which is disposed a fine mesh
15 secured to the frame.
3. An adaptor of claim 1 or claim 2, wherein the or each said peripheral frame is made by injection moulding a thermoplastics material around a mesh such that a peripheral edge portion of the mesh is embedded in the moulded frame.
20
4. An adaptor of any of claims 1 to 3, wherein the mesh has a pore size of from 40 to 400 μ m.
5. An adaptor of any of claims 1 to 4, wherein the mesh is made of
25 polyamide.
6. An adaptor of any of claims 1 to 5, which further comprises locking means to hold the lid in the closed position.
- 30 7. An adaptor of claim 6, wherein the locking means comprises a male member on one of the base and the lid and a female member on the other of the base and the lid and adapted to engage lockingly with the male member.

8. An adaptor of claim 7, wherein the male member comprises a continuous or discontinuous upstanding rib extending around a peripheral area of one of the base and the lid and the female member comprises a continuous or discontinuous groove extending around a peripheral area of the other of the base and the lid and in which the flange is a press fit.

9. An adaptor of any of claims 1 to 8, wherein the base and the lid are interconnected by hinge means.

10. An adaptor of claim 9, wherein the hinge means comprises mesh in one piece with the mesh of the at least one of the base and the lid comprising mesh.

11. An adaptor of any of claims 1 to 10, wherein the base and the lid are adapted to engage in two different relative positions, in one of which positions the height of the chamber is relatively large and in the other of which it is relatively low.

12. An adaptor of claim 11 wherein

(a) in one of the positions the lid engages the base with a first side of the lid facing thereto and in the other of the positions engages the base with a second side of the lid opposite the first facing the base, or

(b) in one of the positions the base engages the lid with a first side of the base facing thereto and in the other of the positions engages the lid with a second side of the base opposite the first facing the lid, or

(c) at least when the lid and the base are hinged together, in one of the positions the lid and the base interengage with a first side of the lid facing a first side of the base and in the other of the positions they interengage with a second side of the lid facing a second side of the base.

13. An adaptor of claim 12(a), wherein the cross wall of the lid is disposed closer to one of said sides of the lid than to the other.
- 5 14. An adaptor of claim 12(b), wherein the cross wall of the base is disposed closer to one of said sides of the base than to the other.
15. An adaptor of claim 12(c), wherein the cross wall of at least one of the base and the lid is disposed closer to one of its sides than to the other.
- 10 16. An adaptor of any of claims 1 to 15 which, when the lid engages the base, has overall dimensions of about 5 mm x 25 mm x 32 mm, or less.
- 15 17. A tissue sample holder, comprising a base and a lid to engage the base and define therewith a chamber to hold a tissue sample, the base having a cross wall which forms the bottom wall of the chamber and the lid having a cross wall which forms the top wall of the chamber, at least one of said cross walls being a perforate, and the base and the lid being adapted to engage in two different relative positions, in one of which positions the height of the chamber is relatively large and in the other of which the height of the chamber is relatively small.
- 20 18. A holder of claim 18, wherein the or each perforate cross wall comprises a fine mesh.
- 25 19. A holder of claim 19, wherein the or each perforate cross wall comprises a frame defining therewithin an area spanned by the mesh, the mesh being secured to the frame.
- 30 20. A holder of any of claims 17 to 19 which further comprises the feature(s) of one or more of claims 6 to 16 or of claim 19 which further comprises the feature(s) of one or more of claims 1 to 5.
21. A capsule for transporting small tissue samples and for processing them in

a processing cassette, the capsule being adapted to fit in a processing cassette and comprising a base and a lid to engage the base, the cross wall of at least one of the lid and the base comprising a fine mesh.

5 22. A capsule of claim 21, wherein both the lid and the base have a cross wall comprise a fine mesh.

23. A capsule of claim 22, which further comprises the features of one or more of claims 2 to 5.

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24. A capsule of claim 22 or claim 23, which further comprises the features of one or more of claims 6 to 16.

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25. A holder for tissue samples, comprising a base and a lid to engage the base, the cross wall of at least one of the lid and the base being perforate and the lid and the base being capable of being interengaged in two different relative positions to form chambers of different height in the capsule.

20

26. A holder of claim 25 which is adapted to fit in a processing cassette.

27. A holder of claim 25, or claim 26 wherein the or each perforate cross wall comprises a fine mesh.

25

28. A holder of claim 27 which further comprises the features of one or more of claims 2 to 5.

29. A holder of any of claims 25 to 28 which further comprises the features of one or more of claims 6 to 16.

30

30. A method of transporting a tissue sample, comprising placing it in a container consisting of an adaptor as defined in any of claims 1 to 16, a holder as defined in any of claims 17 to 20 or 25 to 29 or a capsule as defined in any of

claims 21 to 24, closing the container and transporting it.

5 31. A method of processing a tissue sample prior to infiltrating it with wax for slicing and histological study, comprising placing into a processing cassette a tissue sample contained in an adaptor as defined in any of claims 1 to 16 or a capsule as defined in any of claims 21 to 24, closing the processing cassette, and contacting the processing cassette with processing liquids.

10 32. A method of processing a tissue sample prior to infiltrating it with wax for slicing and histological study, comprising contacting with processing liquids a tissue sample contained in a holder as defined in any of claims 17 to 20 or 25 to 29.

15 33. The use of an adaptor as defined in any of claims 1 to 16 or a capsule as defined in any of claims 21 to 24 as an insert for a histology processing cassette.

34. The use of a container as defined in claim 30 to transport histology samples or to process them prior to infiltration with wax.

20 35. A combination of a histology processing cassette and, contained therein, an adaptor as defined in any of claims 1 to 16 or a capsule as defined in any of claims 21 to 24.

Relevant Technical Fields

- (i) UK Cl (Ed.M) G1B (BCH)
(ii) Int Cl (Ed.5) G01N 1/28, 1/30

Search Examiner
M R WENDT

Date of completion of Search
28 JUNE 1994

Databases (see below)

(i) UK Patent Office collections of GB, EP, WO and US patent specifications.

Documents considered relevant following a search in respect of Claims :-
1-35

(ii) ONLINE DATABASES: WPI, CLAIMS

Categories of documents

- X: Document indicating lack of novelty or of inventive step. P: Document published on or after the declared priority date but before the filing date of the present application.
Y: Document indicating lack of inventive step if combined with one or more other documents of the same category. E: Patent document published on or after, but with priority date earlier than, the filing date of the present application.
A: Document indicating technological background and/or state of the art. &: Member of the same patent family; corresponding document.

Category	Identity of document and relevant passages		Relevant to claim(s)
X	GB 1483574	(TRIANGLE BIOMED) see Figure 1 and Claim 1	1,21,30,31
X	EP 0139424 A2	(PELAM) & US 4569647 see Abstract and Claim 1	1,21,30,31
X	EP 0138351 A2	(PELAM) & US 4557903 see Figure 3. Abstract Claim 1	1,21,30,31
X	US 4997100	(DUDEK) see Figure 1 Abstract Claim 1	1,21,30,31
X	US 4421246	(ALLIED) see Figure 1 Claim 1	1,21,30,31
X	US 4034884	(MILES) see Figure 1 Abstract	1,21,30,31

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